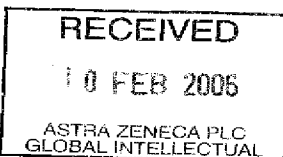


PATENT COOPERATION TREATY

LCP

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY



PCT

To:

GLOBAL INTELLECTUAL PROPERTY
AstraZeneca AB
SE-151 85 Södertälje
SUEDE

CODE	DATE	NTD	
ANKOR	08 FEB 2006		QIPS
DATA ENTERED			
FINAL CHECK			

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing
(day/month/year) 06.02.2006

Applicant's or agent's file reference
101256-1 WO

IMPORTANT NOTIFICATION

International application No.
PCT/GB2004/004784

International filing date (day/month/year)
15.11.2004

Priority date (day/month/year)
17.11.2003

Applicant
ASTRAZENECA AB

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Brell, E

Tel. +49 89 2399-6724



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

CODE	DATE	NTD
ANKOM 08 FEB 2006 GIPS		
DATA ENTERED		
FINAL CHECK		

Applicant's or agent's file reference 101256-1 WO	FOR FURTHER ACTION		See Form PCT/PEA416
International application No. PCT/GB2004/004784	International filing date (day/month/year) 15.11.2004	Priority date (day/month/year) 17.11.2003	
International Patent Classification (IPC) or national classification and IPC A61K31/506, C07D403/12, C07D409/14, C07D495/04, C07D487/04, C07D471/04, C07D401/14, C07D417/04, C07D403/14, A61P35/00			
Applicant ASTRAZENECA AB			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p style="margin-left: 20px;">a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p style="margin-left: 20px;">b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 27.07.2005		Date of completion of this report 06.02.2006	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Grassi, D Telephone No. +49 89 2399-8499	



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/004784

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-129 as originally filed

Claims, Numbers

1-28 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/004784

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18-20,28

because:

☒ the said international application, or the said claims Nos. (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/004784

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	12,15,18,22,25
	No: Claims	1-11,13,14,16,17,19-21,23,24,26-28
Inventive step (IS)	Yes: Claims	
	No: Claims	1-28
Industrial applicability (IA)	Yes: Claims	1-17,21-27
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/GB2004/004784

Reference is made to the following documents:

- D1: WO 03/048133 (cited in the application)
- D2: WO 01/60816

Re Item III

Claims 18-20 and 28 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

- 1) The subject-matter of present claims 1-11 and 13, 14, 16, 17, 19-21, 23, 24 and 26-28 is not new (Article 33(2) PCT).

The document D1 relates to (IGF-1R) tyrosine kinase inhibitors for the treatment of proliferative diseases as cancer (cf. page 18, 58 and 59). Consequently, D1 belongs to the same technical field as the present application and solves a closely related technical problem.

Due to the proviso, the present claims are novel over the examples of D1 (cf. examples 44, 45, 92). However, the subject-matter of the present claim 1-11 essentially overlaps the group of compounds defined in claim 8 of D1.

The range of the overlap can not be regarded as novel, because there is no new technical teaching in the range of the overlap and, as shown by the various examples falling within the scope of the present claims, the skilled person would seriously contemplate applying the technical teaching of D1 in the range of the overlap. Therefore the whole range of the overlap is not novel.

Considering the activity, the intended use and the preparation of the compounds of D1 (cf. pages 15 and 18-22), the claims 13, 14, 16, 17, 19-21, 23, 24 and 26-28 are also not novel.

- 1.1) The subject-matter of the present claims is seen as novel selection from the teaching of D2 for the following reasons.

While there is an overlap between the subject of the present claims and the group of compounds defined by claim 1 of D2 (R2 is NHR5 and R5 is alkyl substituted with aryl), there are no examples in D2 showing the said feature. Therefore, the subject-matter of the present claims is regarded as novel selection from the disclosure of D2.

- 2) The subject-matter of claims 12, 15, 18, 22, 25 and the novel part of claims 1-11 and 13, 14, 16, 17, 19-21, 23, 24 and 26-28 does not involve an inventive step (Article 33(3) PCT).

D2 represents the closest prior art and relates to inhibitor of tyrosine kinases as IGF-1 and TRKA (cf. page 18, example 24 and tables 2, 3).

The subject-matter of claim 1 consists in the selection of a of a group of compounds from the group described in document D2 (cf. above). Such a selection can only be regarded as inventive, if the selection presents unexpected effects or properties in relation to the rest of the range (cf. examples 1, 5-9 or 33-35). However, no such effects or properties are indicated in the application. Hence, no inventive step is present in the subject-matter of the claims.